

REMARKS

Reconsideration is requested.

Claims 1-74 have been canceled, without prejudice. Claims 75-85 are pending.

The claims have been amended to advance prosecution, without prejudice.

The attached Request for Continued Examination (RCE) is being filed to insure consideration of the attached art and Information Disclosure Statement. Return of an initialed copy of the attached PTO-1449 Form, pursuant to MPEP § 609, is requested.

To the extent not obviated by the above, the Section 112, first paragraph "written description", rejection of claims 75-85 is traversed. Reconsideration and withdrawal of the Section 112, first paragraph, rejection of claims 75-85 is requested in view of the following.

The Examiner's indication that "Claims directed to [the]...specific SEQ ID NO's [indicated on page 3 of the Office Action dated March 1, 2004 (Paper No. 0204)] would meet the written description provisions of 35 USC 112, first paragraph." is noted See, page 3 of Paper No. 0204. The claims have been amended with the Examiner's comments in mind and in a manner which is believed to be adequately described by the present specification. Specifically, the objected to term "unique" has been deleted.

The Examiner is further urged to appreciate however that the present invention provides new HCV sequences from unknown HCV types and/or subtypes. These new HCV genotypes are initially identified as one or a few HCV nucleic acid sequences of an isolate that are the "prototype" sequences for the HCV genotype. This is generally known in the art, as described, for example, on page 1, lines 27-29, of the application. The Examiner is also requested to see the legend of Table 1, on page 10 of the

application, which describes a comparison with "other" prototypes isolates. Known prototypes are also given in Table 3, on page 13 of the application as filed. Once a new HCV type or subtype is identified, any person skilled in the art is easily capable of classifying nucleic acid sequences of further isolates of the new type or subtype by methods commonly known in the field of HCV. This is discussed, for example, on page 10, line 13, to page 13, line 12, of the application as filed. The prototype sequences of the new HCV types or subtypes of the present invention are defined by the SEQ ID NOs as identified in amended claim 75. Basis for the SEQ ID NOs can be found in pending claim 76 and in Figure 3.

Moreover, basis for the "at least 5 nucleotides" of the amended claims may be found, for example, at page 8, line 1 of the specification. No new matter has been added. The specific amino acid positions deleted from the list of claim 77 have been deleted in view of the applicants co-pending application Serial No. 08/362,455. Attached for the Examiner's convenience is a copy of the pending claims from the co-pending application.

The claims are submitted to be supported by an adequate written description. Entry of the above amendments and withdrawal of the Section 112, first paragraph "written description", rejection are requested.

To the extent not obviated by the above, the Section 112, second paragraph, rejection of claims 75-85, is traversed. Reconsideration and withdrawal of the rejection are requested in view of the following comments.

As noted above, the objected-to term "unique" has been deleted, to advance prosecution. The claims provide polynucleic acid sequences which will be recognized

by one of ordinary skill in the art as providing prototype sequences for HCV type and subtypes. The previously-submitted claims of U.S. Patent Nos. 5,514,539; 5,882,852 and 6,548,244 are evidence that the Patent Office and those of ordinary skill in the art are well aware of the use of such prototype sequences. Moreover, claims 76 and 78 recite the presence of at least 5 nucleotides of the specified SEQ ID NOs comprising a triplet of nucleotides identified by the applicants as encoding the recited amino acid residues which are specific for the new HCV types or subtypes of the invention. As such, a minimum length of the part is defined in addition to a unique triplet of nucleotides derived from the SEQ ID NOs as specified in the claim.

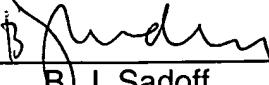
The claims are submitted to be definite and withdrawal of the Section 112, second paragraph, rejection of claims 75-85, is requested.

The claims are submitted to be in condition for allowance and a Notice to that effect is requested. The Examiner is requested to contact the undersigned in the event anything further is required in this regard.

Respectfully submitted,

NIXON & VANDERHYE P.C.

By:


B.J. Sadoff
Reg. No. 36,663

BJS:pp
1100 North Glebe Road, 8th Floor
Arlington, VA 22201-4714
Telephone: (703) 816-4000
Facsimile: (703) 816-4100



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of

MAERTENS et al.

Atty. Ref.: 2551-125

Serial No. 08/362,455

Group: 1631

Filed: January 11, 1995

Examiner: Martinell, J.

For: NEW SEQUENCES OF HEPATITIS C VIRUS
GENOTYPES AND THEIR USE AS
THERAPEUTIC AND DIAGNOSTIC AGENTS

* * * * *

June 1, 2004

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

PENDING CLAIMS IN ABOVE-IDENTIFIED APPLICATION

34. A recombinant vector comprising a vector sequence; and a prokaryotic, eukaryotic or viral promoter sequence operably linked to a polynucleic acid sequence of any of claims 41, 43 to 46 or 48 to 52 or 54 to 70.

39. A kit for determining the presence of HCV genotypes comprising a polynucleic acid sequence according to any one of claims 41, 43 to 46 or 48 to 52 or 54 to 70.

41. An isolated Hepatitis C virus polynucleic acid selected from the group consisting of:

(i) the nucleotide sequences of SEQ ID NO: 13, 15, 17, 19, 21, 23, 25 or 27,

Pending claims of co-pending U.S. Patent Application of **MAERTENS et al.**
Serial No. 08/362,455

(ii) at least 8 contiguous nucleotides of a nucleotide sequence of (i) having at least one genotype-specific nucleotide from the region spanning positions 417 to 957 of the Core/E1 region of HCV subtype 3a, and,

(iii) the complement of the nucleotide sequence of (i) or (ii).

43. An isolated Hepatitis C virus polynucleic acid selected from the group consisting of:

(i) the nucleotide sequence of SEQ ID NO: 29,

(ii) at least 8 contiguous nucleotides of a nucleotide sequence of (i) having at least one genotype-specific nucleotide from the region spanning positions 4664 to 4730 of the NS3 region of HCV subtype 3a, and,

(iii) the complement of the nucleotide sequence of (i) or (ii).

44. An isolated Hepatitis C virus polynucleic acid selected from the group consisting of:

(i) a nucleotide sequence selected from the group consisting of SEQ ID NOs: 31, 33, 35, 37 and 39,

(ii) at least 8 contiguous nucleotides of a nucleotide sequence of (i) having at least one genotype-specific nucleotide from the region spanning positions 4892 to 5292 of the NS3/NS4 region of the HCCI53 isolate of HCV subtype 3a, and,

(iii) the complement of the nucleotide sequence of (i) or (ii).

45. An isolated Hepatitis C virus polynucleic acid selected from the group consisting of:

Pending claims of co-pending U.S. Patent Application of *MAERTENS et al.*
Serial No. 08/362,455

(i) a nucleotide sequence selected from the group consisting of SEQ ID NOs: 5,

7, 1, 3, 9 and 11,

(ii) at least 8 contiguous nucleotides of a nucleotide sequence of (i) having at least one genotype-specific nucleotide from the region spanning positions 8023 to 8192 of the NS5 region of the BR36 subgroup of HCV subtype 3a, and,

(iii) the complement of the nucleotide sequence of (i) or (ii).

46. An isolated Hepatitis C virus polynucleic acid selected from the group consisting of:

(i) a nucleotide sequence selected from the group consisting of SEQ ID NOs: 5, 7, 1, 3, 9 and 11,

(ii) at least 8 contiguous nucleotides of a nucleotide sequence of (i) having at least one genotype-specific nucleotide from the region spanning positions 8023 to 8235 of the NS5B region of HCV subtype 3a, and,

(iii) the complement of the nucleotide sequence of (i) or (ii).

48. An isolated Hepatitis C virus polynucleic acid selected from the group consisting of:

(i) a nucleotide sequence selected from the group consisting of SEQ ID NOs: 41, 43, 45, 47, 49, 51, 53 and 151,

(ii) at least 8 contiguous nucleotides of a nucleotide sequence of (i) having at least one genotype-specific nucleotide from the region spanning positions 1 to 957 of the Core/E1 region of HCV type 5, and,

(iii) the complement of the nucleotide sequence of (i) or (ii).

49. An isolated Hepatitis C virus polynucleic acid selected from the group consisting of:

- (i) a nucleotide sequence selected from the group consisting of SEQ ID NOs: 197 and 199,
- (ii) at least 8 contiguous nucleotides of a nucleotide sequence of (i) having at least one genotype-specific nucleotide from the region spanning positions 3856 to 4209 of the NS3 region of HCV type 5, and,
- (iii) the complement of the nucleotide sequence of (i) or (ii).

50. An isolated Hepatitis C virus polynucleic acid selected from the group consisting of:

- (i) the nucleotide sequence of SEQ ID NO:157,
- (ii) at least 8 contiguous nucleotides of a nucleotide sequence of (i) having at least one genotype-specific nucleotide from the region spanning positions 980 to 1179 of the E1/E2 region of HCV type 5, and,
- (iii) the complement of the nucleotide sequence of (i) or (ii).

51. An isolated Hepatitis C virus polynucleic acid selected from the group consisting of:

- (i) a nucleotide sequence selected from the group consisting of SEQ ID NOs: 59 and 61,
- (ii) at least 8 contiguous nucleotides of a nucleotide sequence of (i) having at least one genotype-specific nucleotide from the region spanning positions 4936 to 5292 of the NS4 region of HCV type 5, and,
- (iii) the complement of the nucleotide sequence of (i) or (ii).

Pending claims of co-pending U.S. Patent Application of **MAERTENS et al.**
Serial No. 08/362,455

52. An isolated Hepatitis C virus polynucleic acid selected from the group consisting of :

- (i) a nucleotide sequence selected from the group consisting of SEQ ID NOs: 159 and 161,
- (ii) at least 8 contiguous nucleotides of a nucleotide sequence of (i) having at least one genotype-specific nucleotide spanning positions 7932 to 8271 of the NS5B region of the BE95 and BE96 subgroup of HCV subtype 5a, and,
- (iii) the complement of the nucleotide sequence of (i) or (ii).

54. An isolated Hepatitis C virus polynucleic acid selected from the group consisting of :

- (i) a nucleotide sequence selected from the group consisting of SEQ ID NOs: 183, 185, 118 and 187,
- (ii) at least 8 contiguous nucleotides of a nucleotide sequence of (i) having at least one genotype-specific nucleotide spanning positions 379 to 957 of the E1 region of HCV subtype 4c, and,
- (iii) the complement of the nucleotide sequence of (i) or (ii).

55. An isolated Hepatitis C virus polynucleic acid selected from the group consisting of :

- (i) the nucleotide sequence of SEQ ID NO:189,
- (ii) at least 8 contiguous nucleotides of a nucleotide sequence of (i) having at least one genotype-specific nucleotide spanning positions 379 to 957 of the E1 region of HCV subtype 4a, and,
- (iii) the complement of the nucleotide sequence of (i) or (ii).

56. An isolated Hepatitis C virus polynucleic acid selected from the group consisting of :

- (i) a nucleotide sequence selected from the group consisting of SEQ ID NOs: 167, 122 and 169,
- (ii) at least 8 contiguous nucleotides of a nucleotide sequence of (i) having at least one genotype-specific nucleotide spanning positions 379 to 957 of the E1 region of HCV subtype 4e, and,
- (iii) the complement of the nucleotide sequence of (i) or (ii).

57. An isolated Hepatitis C virus polynucleic acid selected from the group consisting of :

- (i) a nucleotide sequence selected from the group consisting of SEQ ID NOs: 171 and 173,
- (ii) at least 8 contiguous nucleotides of a nucleotide sequence of (i) having at least one genotype-specific nucleotide spanning positions 379 to 957 of the E1 region of HCV subtype 4f, and,
- (iii) the complement of the nucleotide sequence of (i) or (ii).

58. An isolated Hepatitis C virus polynucleic acid selected from the group consisting of :

- (i) a nucleotide sequence selected from the group consisting of SEQ ID NOs: 175 and 120,
- (ii) at least 8 contiguous nucleotides of a nucleotide sequence of (i) having at least one genotype-specific nucleotide spanning positions 379 to 957 of the E1 region of HCV subtype 4g, and,

(iii) the complement of the nucleotide sequence of (i) or (ii).

59. An isolated Hepatitis C virus polynucleic acid selected from the group consisting of :

(i) the nucleotide sequence of SEQ ID NO:177,
(ii) at least 8 contiguous nucleotides of a nucleotide sequence of (i) having at least one genotype-specific nucleotide spanning positions 379 to 957 of the E1 region of HCV subtype 4h, and,

(iii) the complement of the nucleotide sequence of (i) or (ii).

60. An isolated Hepatitis C virus polynucleic acid selected from the group consisting of :

(i) the nucleotide sequence of SEQ ID NO:179,
(ii) at least 8 contiguous nucleotides of a nucleotide sequence of (i) having at least one genotype-specific nucleotide spanning positions 379 to 957 of the E1 region of HCV subtype 4i, and,

(iii) the complement of the nucleotide sequence of (i) or (ii).

61. An isolated Hepatitis C virus polynucleic acid selected from the group consisting of :

(i) the nucleotide sequence of SEQ ID NO:181,
(ii) at least 8 contiguous nucleotides of a nucleotide sequence of (i) having at least one genotype-specific nucleotide spanning positions 379 to 957 of the E1 region of the CAR4/901 subgroup of HCV type 4, and,

(iii) the complement of the nucleotide sequence of (i) or (ii).

Pending claims of co-pending U.S. Patent Application of *MAERTENS et al.*
Serial No. 08/362,455

62. An isolated Hepatitis C virus polynucleic acid selected from the group consisting of :

- (i) a nucleotide sequence selected from the group consisting of SEQ ID NOs: 106, 108, 110 and 112 ,
- (ii) at least 8 contiguous nucleotides of a nucleotide sequence of (i) having at least one genotype-specific nucleotide spanning positions 7932 to 8271 of the NS5 region of HCV subtype 4c, and,
- (iii) the complement of the nucleotide sequence of (i) or (ii).

63. An isolated Hepatitis C virus polynucleic acid selected from the group consisting of :

- (i) a nucleotide sequence selected from the group consisting of SEQ ID NOs: 116 and 201,
- (ii) at least 8 contiguous nucleotides of a nucleotide sequence of (i) having at least one genotype-specific nucleotide spanning positions 7932 to 8271 of the NS5 region of HCV subtype 4e, and,
- (iii) the complement of the nucleotide sequence of (i) or (ii).

64. An isolated Hepatitis C virus polynucleic acid selected from the group consisting of :

- (i) the nucleotide sequence of SEQ ID NO:203 ,
- (ii) at least 8 contiguous nucleotides of a nucleotide sequence of (i) having at least one genotype-specific nucleotide spanning positions 7932 to 8271 of the NS5 region of HCV subtype 4f, and,
- (iii) the complement of the nucleotide sequence of (i) or (ii).

Pending claims of co-pending U.S. Patent Application of *MAERTENS et al.*
Serial No. 08/362,455

65. An isolated Hepatitis C virus polynucleic acid selected from the group consisting of :

(i) the nucleotide sequence of SEQ ID NO : 114,
(ii) at least 8 contiguous nucleotides of a nucleotide sequence of (i) having at least one genotype-specific nucleotide spanning positions 7932 to 8271 of the NS5 region of HCV subtype 4g, and,

(iii) the complement of the nucleotide sequence of (i) or (ii).

66. An isolated Hepatitis C virus polynucleic acid selected from the group consisting of :

(i) the nucleotide sequence of SEQ ID NO:207,
(ii) at least 8 contiguous nucleotides of a nucleotide sequence of (i) having at least one genotype-specific nucleotide spanning positions 7932 to 8271 of the NS5 region of HCV subtype 4h, and,

(iii) the complement of the nucleotide sequence of (i) or (ii).

67. An isolated Hepatitis C virus polynucleic acid selected from the group consisting of :

(i) the nucleotide sequence of SEQ ID NO:209,
(ii) at least 8 contiguous nucleotides of a nucleotide sequence of (i) having at least one genotype-specific nucleotide spanning positions 7932 to 8271 of the NS5 region of HCV subtype 4i, and,

(iii) the complement of the nucleotide sequence of (i) or (ii).

68. An isolated Hepatitis C virus polynucleic acid selected from the group consisting of :

Pending claims of co-pending U.S. Patent Application of *MAERTENS et al.*
Serial No. 08/362,455

(i) the nucleotide sequence of SEQ ID NO: 211,
(ii) at least 8 contiguous nucleotides of a nucleotide sequence of (i) having at least one genotype-specific nucleotide spanning positions 7932 to 8271 of the NS5 region of HCV subtype 4j, and,
(iii) the complement of the nucleotide sequence of (i) or (ii).

69. An isolated Hepatitis C virus polynucleic acid selected from the group consisting of :

(i) the nucleotide sequences of SEQ ID NO:143,
(ii) at least 8 contiguous nucleotides of a nucleotide sequence of (i) having at least one genotype-specific nucleotide spanning positions 379 to 957 of the Core/E1 region of HCV subtype 2d, and,
(iii) the complement of the nucleotide sequence of (i) or (ii).

70. An isolated Hepatitis C virus polynucleic acid selected from the group consisting of :

(i) the nucleotide sequence of SEQ ID NO: 145,
(ii) at least 8 contiguous nucleotides of a nucleotide sequence of (i) having at least one genotype-specific nucleotide spanning positions 7932 to 8271 of the NS5B region of HCV subtype 2d, and,
(iii) the complement of the nucleotide sequence of (i) or (ii).

73. A method of detecting or screening for one or more HCV genotypes present in a biological sample, comprising the following steps:

(i) providing a sample nucleic acid,

Pending claims of co-pending U.S. Patent Application of *MAERTENS et al.*
Serial No. 08/362,455

(ii) determining the presence of a polynucleic acid sequence according to any of claims 41, 43 to 46 or 48 to 52 or 54 to 70, by means of a sequencing reaction, and,
(iii) inferring from the presence of one or more of these HCV polynucleic acid sequences of step (ii) the genotype(s) present in said sample.

74. A method of detecting or screening for one or more HCV genotypes present in a biological sample, comprising the following steps:

(i) providing a sample nucleic acid,
(ii) specifically amplifying a polynucleic acid sequence according to any of claims 41, 43 to 46 or 48 to 52 or 54 to 70, and,
(iii) inferring from the presence of one or more amplified HCV polynucleic acid sequences of step (ii) the genotype(s) present in said sample.

75. An isolated HCV polynucleic acid according to any of claims 41, 43 to 46 or 48 to 52 or 54 to 70, wherein said polynucleic acid is capable of acting as a primer for HCV type- or subtype-specific amplification.

76. An isolated HCV polynucleic acid according to any of claims 41, or 43 to 46, wherein said polynucleic acid is capable of acting as a primer for specific amplification of the BR36 subgroup of HCV subtype3a.

78. An isolated HCV polynucleic acid according to any of claims 54 to 68, wherein said polynucleic acid is capable of acting as a primer for specific amplification of HCV type 4.

Pending claims of co-pending U.S. Patent Application of *MAERTENS et al.*
Serial No. 08/362,455

79. An isolated HCV polynucleic acid according to any of claims 48 to 52,
wherein said polynucleic acid is capable of acting as a primer for specific amplification of
HCV type 5.

80. An isolated HCV polynucleic acid according to any of claims 69 to 70,
wherein said polynucleic acid is capable of acting as a primer for specific amplification of
HCV subtype 2d.

81. An isolated HCV polynucleic acid according to any of claims 41, 43 to 46 or
48 to 52 or 54 to 70, wherein said polynucleic acid is capable of acting as a probe for
HCV type- or subtype-specific hybridisation.

82. An isolated HCV polynucleic acid according to any of claims 41, or 43 to
46, wherein said polynucleic acid is capable of acting as a probe for specific
hybridisation to a HCV subtype 3a nucleic acid sequence from the BR36 subgroup.

84. An isolated HCV polynucleic acid according to any of claims 69 to 70,
wherein said polynucleic acid is capable of acting as a probe for specific hybridisation to
a HCV subtype 2d nucleic acid sequence.

85. An isolated HCV polynucleic acid according to any of claims 48 to 52,
wherein said polynucleic acid is capable of acting as a probe for specific hybridisation to
a HCV type 5 nucleic acid sequence.

Pending claims of co-pending U.S. Patent Application of **MAERTENS et al.**
Serial No. 08/362,455

86. An isolated HCV polynucleic acid according to any of claims 54 to 68,
wherein said polynucleic acid is capable of acting as a probe for specific hybridisation to
a HCV type 4 nucleic acid sequence.

87. A method for detecting HCV nucleic acids present in a biological sample
comprising the following steps:

- (i) providing a sample nucleic acid,
- (ii) determining the sequence of one or more HCV polynucleic acids according to
any of claims 41, 43 to 46 or 48 to 52 or 54 to 70 present in said sample.